

**Amendments to the Claims**

1. (Withdrawn; Previously amended) A method for producing a vaccine formulation for oral administration, said method comprising:

coacervating at least one antigen with a biodegradable polymer to provide microparticles sized such that at least 50% of the microparticles are less than 5  $\mu\text{m}$ , the microparticles comprising the at least one antigen entrapped or encapsulated by the biodegradable polymer; and

combining a pharmaceutically effective amount of said microparticles with a pharmaceutically acceptable carrier to provide said vaccine formulation for oral administration.

2. (Withdrawn; Previously amended) The method of Claim 1, wherein the microparticles are sized such that at least 50% of the microparticles are less than 3  $\mu\text{m}$ .

3. (Withdrawn; Previously amended) The method of Claim 1, wherein the biodegradable polymer comprises a copolymer of lactic acid or an enantiomer of lactic acid with glycolic acid or an enantiomer of glycolic acid.

4. (Canceled)

5. (Withdrawn; Previously amended) The method of Claim 1, wherein the antigen comprises a *B. pertussis* antigen.

6. (Withdrawn; Previously amended) The method of Claim 1, wherein the microparticles comprise at least 2 subpopulations of microparticles, each subpopulation comprising a different antigen entrapped or encapsulated by a biodegradable polymer.

7. (Withdrawn; Previously amended) A method for producing a vaccine formulation for oral administration, said method comprising:

coacervating at least one antigen with a biodegradable polymer to provide nanoparticles sized such that at least 50% of the nanoparticles are less than 600nm, the nanoparticles comprising the at least one antigen entrapped or encapsulated by the biodegradable polymer; and

combining a pharmaceutically effective amount of said nanoparticles with a pharmaceutically acceptable carrier to provide said vaccine formulation for oral administration.

8. (Withdrawn; Previously amended) The method of Claim 7, wherein the nanoparticles are sized such that at least 50% of the nanoparticles are less than 500 nm.

9. (Withdrawn; Previously amended) The method of Claim 7, wherein the biodegradable polymer comprises a copolymer of lactic acid or an enantiomer of lactic acid with glycolic acid or an enantiomer of glycolic acid.

10. (Canceled)

11. (Withdrawn; Previously amended) The method of Claim 7, wherein the antigen comprises a *B. pertussis* antigen.

12. (Withdrawn; Previously amended) The method of Claim 7, wherein the nanoparticles comprise at least 2 subpopulations of nanoparticles, each subpopulation comprising a different antigen entrapped or encapsulated by a biodegradable polymer.

13 to 20. (Canceled)

21. (Currently amended) A method of inducing a protective immune response, said method comprising orally administering to a subject therapeutically effective amounts of at least a first and a second subpopulation of microparticles, wherein each of said microparticles comprises an antigen entrapped or encapsulated by a biocompatible, biodegradable polymer, and wherein the antigen in the microparticles of the first one subpopulation is different than the antigen in the

In re Application of David J. Brayden  
Application No. 09/386,709

Page 4  
July 30, 2003

microparticles of the second subpopulation and at least 50% of the microparticles are less than 5  $\mu\text{m}$ .

22. (Previously amended) The method of claim 21 wherein the microparticles are sized such that at least 50% of the microparticles are less than 3  $\mu\text{m}$ .

23. (Previously amended) The method of claim 21 wherein the biocompatible, biodegradable polymer comprises of lactic acid or an enantiomer of lactic acid with glycolic acid or an enantiomer of glycolic acid.

24. (Currently amended) The method of claim 21 wherein the antigen in the first subpopulation of microparticles is a *B. pertussis* antigen and the antigen in the second ~~first~~ subpopulation of microparticles is a *B. pertussis* antigen.

25. (Previously amended) The method of claim 24 wherein the *B. pertussis* antigens are selected from the group consisting of inactivated pertussis toxin (PTd), filamentous hemagglutinin (FHA) and pertactin.

26. (Canceled)

27. (Previously amended) The method of claim 21 wherein both the antigen in the first subpopulation of microparticles and the antigen in the second subpopulation of microparticles are selected from the group consisting of inactivated pertussis toxin (PTd), filamentous hemagglutinin (FHA) and pertactin.

28. (Currently amended) A method of inducing a protective immune response, said method comprising orally administering to a subject therapeutically effective amounts of at least a first and a second subpopulation of nanoparticles, wherein each of said nanoparticles comprises an antigen entrapped or encapsulated by a biocompatible, biodegradable polymer, and wherein the antigen in the nanoparticles of the first one subpopulation is different than the antigen in the

In re Application of David J. Brayden  
Application No. 09/386,709

Page 5  
July 30, 2003

nanoparticles of the second subpopulation and at least 50% of the nanoparticles are less than 600 nm.

29. (Previously amended) The method of claim 28 wherein the biocompatible, biodegradable polymer comprises a copolymer of lactic acid or an enantiomer of lactic acid with glycolic acid or an enantiomer of glycolic acid.

30. (Currently amended) The method of claim 28 wherein the antigen in the first subpopulation of microparticles is a *B. pertussis* antigen and the antigen in the second ~~first~~ subpopulation of microparticles is a *B. pertussis* antigen.

31. (Previously amended) The method of claim 30 wherein the *B. pertussis* antigen is selected from the group consisting of inactivated pertussis toxin (PTd), filamentous hemagglutinin (FHA) and pertactin.

32. (Canceled)

33. (Previously amended) The method of claim 28 wherein both the antigen in the first subpopulation of microparticles and the antigen in the second subpopulation of microparticles is selected from the group consisting of inactivated pertussis toxin (PTd), filamentous hemagglutinin (FHA) and pertactin.

34. (Canceled)

35. (Currently amended) The method of claim 33 ~~34~~ wherein the biocompatible, biodegradable polymer comprises a copolymer of lactic acid or an enantiomer of lactic acid with glycolic acid or an enantiomer of glycolic acid.

36. (Canceled)

37. (Canceled)

In re Application of David J. Brayden  
Application No. 09/386,709

Page 6  
July 30, 2003

38. (Previously presented) A method of Claim 21 wherein the microparticles in each subpopulation were formed by coacervation.

39. (Previously presented) A method in Claim 28 wherein the nanoparticles in each subpopulation were formed by coacervation.

40. (Canceled)

41. (New) A method of Claim 23 wherein the microparticles in each subpopulation were formed by coacervation.

42. (New) A method in Claim 29 wherein the nanoparticles in each subpopulation were formed by coacervation.